

Notice of Allowability

Application No.

10/018,429

Applicant(s)

BOHLMANN ET AL.

Examiner

Art Unit

Barbara P. Badio, Ph.D.

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to ____.
2. ☒ The allowed claim(s) is/are 1-12 and 14-16.
3. ☐ The drawings filed on ____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: ____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
(a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) ☐ hereto or 2) ☐ to Paper No. ____.
(b) ☐ including changes required by the proposed drawing correction filed ____, which has been approved by the Examiner.
(c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. ____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|--|
| 1 <input type="checkbox"/> Notice of References Cited (PTO-892) | 5 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6 <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No. ____. |
| 3 <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No. ____ | 7 <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8 <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9 <input type="checkbox"/> Other |

Barbara P. Badio, Ph.D.
Primary Examiner
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EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

The specification has been amended as follows:

Page 1, after the Title, the following paragraph has been inserted: --

This application is a 371 of PCT/EP00/05969 filed June 26, 2000.

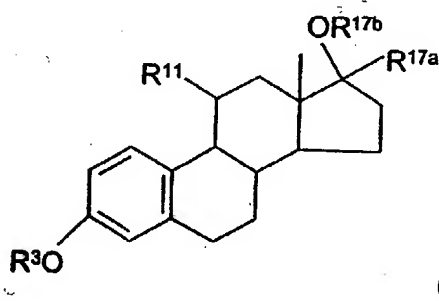
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Authorization for this examiner's amendment was given in a telephone interview with Mr. James Ruland on January 12, 2004.

The application has been amended as follows:

Claim 1 has been amended to read as: --

1. An 11β -substituted estratriene of formula I



in which

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R^3 means a hydrogen atom, a hydrocarbon radical with up to 8 carbon atoms or a radical of partial formula $R^3-C(O)-$, in which R^3 means a hydrogen atom or a hydrocarbon radical with up to 8 carbon atoms or a phenyl radical,

R^{11} means a radical of formula $-A-B-Z-R^{20}$,

in which

A stands for a direct bond, and

B stands for a straight-chain or branched-chain alkylene, alkenylene or alkynylene group with 4, 5 or 6 carbon atoms,

Z stands for $-NR^{21}-$ and R^{21} stands for a C_1 - C_3 alkyl group,

whereby R^{20} means

a hydrogen atom,

a straight-chain or branched-chain alkyl, alkenyl or alkynyl group with up to 10 carbon atoms,

$-D-C_nF_{2n+1}$, whereby D is a straight-chain or branched-chain alkylene, alkenylene or alkynylene group with up to 8 carbon atoms and n is an integer from 1 to 8,

$-D$ -aryl, whereby D has the already indicated meaning, and aryl stands for a phenyl, 1- or 2-naphthyl radical or a heteroaryl radical that is optionally substituted in one or two places,

$-L-CH=CF-C_pF_{2p+1}$, whereby L is a straight-chain or branched-chain alkylene, alkenylene or alkynylene group with up to 7 carbon atoms and p is an integer from 1 to 7,

whereby in the three cases above in D or L, a methylene group can be replaced by a sulfur atom, a sulfone group or a sulfoxide group,

-D-O-(CH₂)_q-aryl, whereby D and aryl have the already indicated meanings, and q is 0, 1, 2 or 3,

-D-O-(CH₂)_r-C_nF_{2n+1}, whereby D and n have the already indicated meanings, and r stands for an integer from 1 to 5,

whereby in addition in all relevant cases above, R²¹ together with D with the inclusion of the nitrogen atom can then form a pyrrolidine ring that is substituted in 2- or 3-position,

or

R²⁰ and R²¹ with the nitrogen atom to which they are bonded form a saturated or unsaturated heterocyclic compound with 5 or 6 chain links, which optionally contains one or two additional heteroatoms, selected from nitrogen, oxygen and sulfur, and optionally is substituted,
and

R^{17a} in α - or β -position means a hydrogen atom, a C₁₋₅ alkyl, a C₂₋₅ alkenyl or a C₂₋₅ alkynyl group or a trifluoromethyl group, or together with the radical OR^{17b} means a keto-oxygen atom, and

R^{17b} means a hydrogen atom or a radical of partial formula R^{17'} --C(O)--, in which

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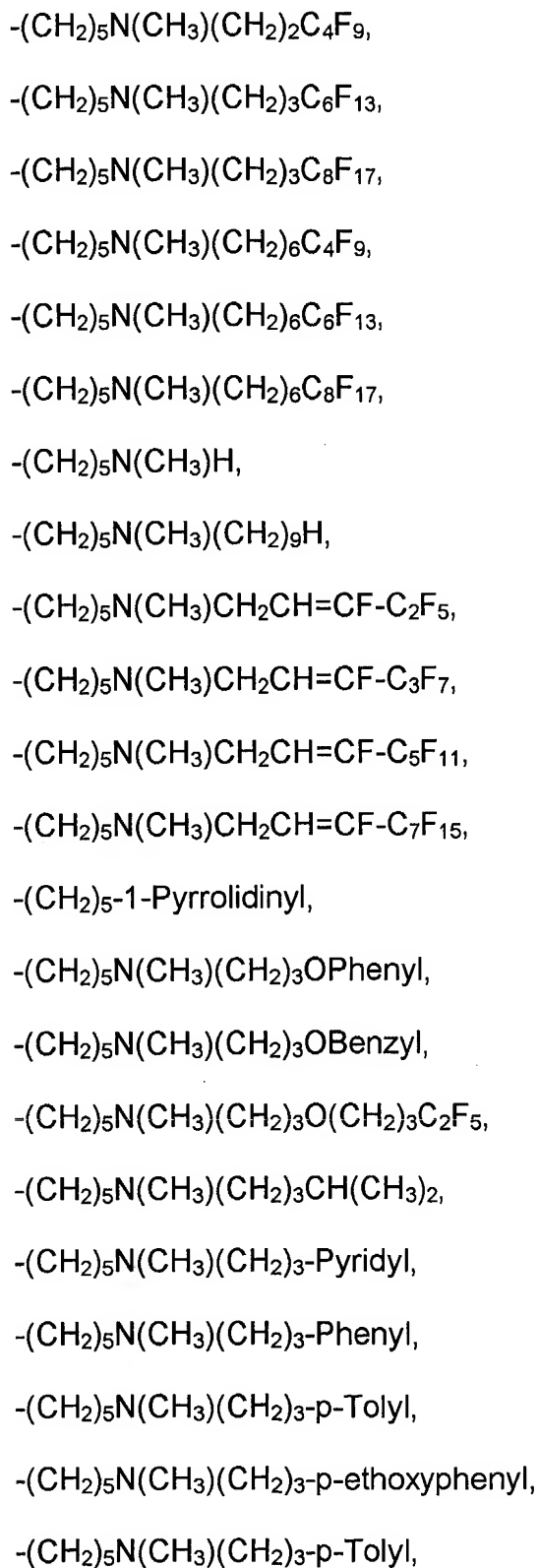
R¹⁷ means a hydrogen atom or a hydrocarbon radical with up to 8 carbon atoms.

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Claim 5 has been amended to read as: --

5. An 11 β -substituted estratriene according to claim 1, in R¹¹ is selected from the group of the following side chains

- (CH₂)₅N(CH₃)-(CH₂)₃-S-(CH₂)₃C₂F₅,
- (CH₂)₅NH-(CH₂)₃-S-(CH₂)₃C₂F₅,
- (CH₂)₅N(CH₃)-(CH₂)₃-S-CH₂-2-Pyridyl,
- (CH₂)₅N(CH₃)-(CH₂)₃-SO-CH₂-2-Pyridyl,
- (CH₂)₅N(CH₃)-(CH₂)₃-S-CH₂-p-CF₃-Phenyl,
- (CH₂)₅N(CH₃)-(CH₂)₃-SO-CH₂-p-CF₃-Phenyl,
- (CH₂)₅-[2-pyrrolidine-1-yl]-CH₂-S-p-CF₃-Phenyl,
- (CH₂)₅-[2-pyrrolidine-1-yl]-CH₂-SO-p-CF₃-Phenyl,
- (CH₂)₅N(CH₃)(CH₂)₃C₂F₅,
- (CH₂)₅N(CH₃)(CH₂)₆C₂F₅,
- (CH₂)₅N(CH₃)(CH₂)₇C₂F₅,
- (CH₂)₅N(CH₃)(CH₂)₈C₂F₅,
- (CH₂)₆N(CH₃)(CH₂)₆C₂F₅,
- (CH₂)₆N(CH₃)(CH₂)₇C₂F₅,
- (CH₂)₆N(CH₃)(CH₂)₈C₂F₅,



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-(CH₂)₅N(CH₃)(CH₂)₃-p-Chlorophenyl, or

-(CH₂)₅N(CH₃)(CH₂)₃-O-CH₂-Phenyl.

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Claim 6 has been amended to read as: --

6. A compound of claim 1 which is

11β-[5-(methyl {3-[(4,4,5,5,5-pentafluoropentyl)sulfanyl]-propyl}amino)pentyl]

estra-1,3,5(10)-triene-3,17β-diol,

11β-(5-{3-[(4,4,5,5,5-pentafluoropentyl)sulfanyl]-propylamino}pentyl]estra-

1,3,5(10)-triene-3,17β-diol,

11β-[5-(methyl {3-[(2-pyridylmethyl)sulfanyl]propyl}-amino)pentyl]estra-1,3,5(10)-

triene-3,17β-diol,

11β-(5-{methyl{3-[(2-pyridylmethyl)sulfonyl]propyl}amino)pentyl]estra-1,3,5(10)-

triene-3,17β-diol,

11β-[5-(methyl {3-[4-trifluoromethyl]benzylsulfanyl]-propyl}-amino)pentyl]estra-

1,3,5(10)-triene-3,17β-diol,

11β-[5-(methyl{3-[4-(trifluoromethyl)benzylsulfinyl]propyl}-amino)pentyl]estra-

1,3,5(10)-triene-3,17β-diol,

11β-{5-[(2S)-2-[[4-(trifluoromethyl)phenyl]sulfanyl-methyl]pyrrolidine-1-

yl]pentyl}estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[(2S)-2-[[4-(trifluoromethyl)phenyl]sulfinyl-methyl]pyrrolidine-1-yl]pentyl}estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[methyl-(8,8,9,9,9-pentafluoro-nonyl)amino]-pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[methyl-nonyl-amino]pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[methyl-(9,9,10,10,10-pentafluoro-decyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{6-[methyl-(8,8,9,9,9-pentafluoro-nonyl)-amino]-hexyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{6-[methyl-(9,9,10,10,10-pentafluoro-decyl)amino]-hexyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-[5-(methyl-amino)-pentyl]-estra-1,3,5(10)-triene-3,17β-diol,

11β-(5-pyrrolidine-1-yl-pentyl)-estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[methyl-(4,4,5,5,5-pentafluoro-pentafluoro-pentyl)-amino]pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[methyl-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-nonyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro-undecyl)-methyl-amino]-pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

11β-{5-[methyl-(3,3,4,4,5,5,6,6,6-nonafluoro-hexyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17β-diol,

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11 β -{5-[methyl-(7,7,8,8,8-pentafluoro-octyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{6-[methyl-(7,7,8,8,8-pentafluoro-octyl)-amino]-hexyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[methyl-(7,7,8,8,9,9,10,10,10-nonafluoro-decyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[methyl-(7,7,8,8,9,9,10,10,11,11,12,12,12-tridecafluoro-dodecyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[(7,7,8,8,9,9,10,10,11,11,12,12,13,13,14,14-heptadecafluoro-tetradecyl)-methyl-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[(3,4,4,5,5,5-hexafluoro-pent-2-enyl)-methyl-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[(3,4,4,5,5,6,6,7,7,8,8,8-dodecafluoro-oct-2-enyl)-methyl-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[(3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-hexadecafluoro-dec-2-enyl)-methyl-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5[methyl(3-phenoxy-propyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[(3-benzyloxy-propyl)-methyl-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

11 β -{5-[N-methyl-N-3-(4,4,5,5,5-pentafluoropentyloxy)-propylamino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,

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11 β -{5-[methyl-2-p-tolyl-ethyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,
11 β -(5- {[2-(4-ethoxy-phenyl)-ethyl]-methyl-amino}-pentyl)-estra-1,3,5(10)-triene-
3,17 β -diol,
11 β -{5-[methyl-(3-phenyl-propyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,
11 β -{5-[methyl-(3-pyridin-3-yl-propyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -
diol,
11 β -{5-[methyl-(3-p-tolyl-propyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol,
11 β -(5-{[3-(4-chloro-phenyl)-propyl]-methyl-amino}-pentyl)-estra-1,3,5(10)-triene-
3,17 β -diol,
11 β -(5-{[3-(4-ethoxy-phenyl)-propyl]-methyl-amino}-pentyl)-estra-1,3,5(10)-triene-
3,17 β -diol, or
11 β {5[methyl-(4-methyl-pentyl)-amino]-pentyl}-estra-1,3,5(10)-triene-3,17 β -diol.

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Claim 11 has been amended to read as: --

11. A method of providing an antiestrogenic action comprising administration an effective amount of a compound according to claim to a patient in need thereof.

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Claim 13 has been cancelled.

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Claim 14 has been amended to read as: --

14. A method of treating osteoporosis, or pre-, peri- or post-menopause comprising administering an effective amount of a compound according to claim 1 to a patient in need thereof.

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Claim 15 has been amended to read as: --

15. A method of providing hormone replacement therapy comprising administering an effective amount of a compound according to claim 1 to a patient in need thereof.

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Telephone Inquiry

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 703-308-4595. The examiner can normally be reached on M-F from 6:00am-3:30pm.

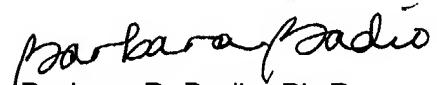
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308- 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

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Note: As of February 2, 2004, the examiner can be reached at (571)-272-0609 and her supervisor at (571)-272-0602.


Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1616

BB
January 14, 2004